Ex 9

EXHIBIT 9

AMENDMENT TO A PENDING APPLICATION

Pharmaceutical Research
2800 Plymouth Road Phone 313 996-8210
Ann Arbor, MI Fax 313 996-8072
48105

PARKE-DAVIS
People Who Care

April 9, 1996

William M. Merino, Ph.D.
Senior Vice President
Worldwide Regulatory Affairs

NDA 20-130
Estrostep® 21
Estrostep® Fe
(norethindrone acetate and ethinyl estradiol tablets, USP)

Re: Amendment to Estrostep NDA
Items 3 and 4

Solomon Sobel, M.D.
Director
Division of Metabolism and Endocrine
Drug Products (HFD-510)
Document Control Room 14B-19
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Sobel:

Reference is made to our New Drug Application (NDA 20-130) for Estrostep® (norethindrone acetate and ethinyl estradiol, USP) Tablets for oral contraception, submitted on December 27, 1990, and its amendments. Reference is also made to your nonapprovable letter of August 27, 1992 (Attachment 1), and our response of September 3, 1992 (Ref. No. 26), notifying you of our intent to amend the application.

According to the August 27, 1992 letter from FDA, FDA could not verify compliance with current good manufacturing practice regulations at the Fajardo, Puerto Rico facility. In addition, FDA requested labeling revisions and reiterated our commitments for Phase 4 studies.

We hereby amend our application addressing the matters described in the August 27, 1992 letter. This amendment contains revised Items 3 Chemistry, Manufacturing and Controls and 4 Samples, Methods Validation, Labeling. The Notes to Reviewer in Item 3.1 summarize the revisions made to the application. Review and archival copies of each section are provided.

The comments relating to current good manufacturing practices described in the August 27, 1992 letter have been addressed. As you are aware, Warner-Lambert is subject to a Consent Decree entered on August 17, 1993. Under the terms of the Consent Decree, Warner-Lambert submitted an independent expert certification to the FDA confirming that the Fajardo facility complies with current Good Manufacturing Practice regulations. The FDA then conducted an intensive inspection of the Fajardo facility and, by letter dated June 20, 1995, stated that the facility is in compliance with 21 U.S.C. § 351(1)(2)(B) and 21 C.F.R. Parts 210 and 211 (see Attachment 2).

Warner-Lambert had also been subject to the FDA Application Integrity Policy (AIP). Warner-Lambert has now received confirmation from FDA (Attachment 3) that the Fajardo, Puerto Rico facility where Estrostep is manufactured, is no longer subject to the AIP.

Since your August 1992 letter we have received a number of labeling updates on our marketed oral contraceptives which are applicable to Estrostep. Therefore, in addition to those changes outlined in your letter, additional updates have been incorporated into the labeling.

There have been no new clinical pharmacology or clinical studies, therefore we have no new safety information to provide. We are still committed to conducting a multiple dose biopharmaceutics study upon approval of the product. We also agreed to update the labeling with the study information once complete.

As this application was submitted before the institution of the Prescription Drug User Fee Act it is not subject to user fees. It is our understanding that pursuant to 21 CFR 314.60, that as a major amendment FDA will act on the application within 180 days.

Pursuant to 21 CFR 314.440, a complete copy of the amendment has been sent to the FDA District Offices in Newark, New Jersey. In addition, a complete copy of the amendment has been sent to the FDA District office in San Juan, Puerto Rico.

If you have any questions regarding Chemistry, Manufacturing and Controls, please contact Leslie Bloom at 313/996-7399 or by FAX at 313/996-7890 or Sean Brennan at 313/996-7596. For all other questions or concerns regarding the application, please contact Mary E. Taylor, MPH at 313/996-5000 or by FAX at 313/998-3283.

Sincerely,

William M. Mering

William M. Mering

WM\lb\rm
t:\nda\20-130\040196.amn

Attachments

cc: Ms. Regina Brown, Newark District Office
Mr. Richard Dent/Mr. Samuel Jones, San Juan District Office

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001
Expiration Date: June 30, 1992
See OMB Statement on Page 3.

FOR FDA USE ONLY	
DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO. ASS.

NOTE: No application may be filed unless a completed application form has been received (21 CFR Part 314).

NAME OF APPLICANT
Parke-Davis Pharmaceutical Research
Division of Warner-Lambert Company

DATE OF SUBMISSION
April 9, 1996

ADDRESS (Number, Street, City, State and Zip Code)
2800 Plymouth Road, P.O. Box 1047
Ann Arbor, MI 48106-1047

TELEPHONE NO. (Include Area Code)
313/996-5210
313/996-5070

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER (If previously issued)
20-130

DRUG PRODUCT

ESTABLISHED NAME (e.g., USP/USAN)
Norethindrone Acetate and Ethinyl Estradiol

PROPRIETARY NAME (if any)
Estrostep® 21
Estrostep® Fe

CODE NAME (if any)
CI-376

CHEMICAL NAME
(17a)-19-Norpregna-1,3,5 (10)-trien-20-yne-3,17- diol and
(17a)-17-(acetyloxy)-19-norpregn-4-en-20-yn-3-one

DOSAGE FORM
Tablets

ROUTE OF ADMINISTRATION
Oral

STRENGTH(S)
1mg/20μg
1mg/30μg
1mg/35μg

PROPOSED INDICATIONS FOR USE
Contraception

LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (21 CFR Part 312), NEW DRUG OR ANTIBIOTIC APPLICATIONS (21 CFR Part 314), AND DRUG MASTER FILES (21 CFR 314.420) REFERRED TO IN THIS APPLICATIONS:

IND 31,861	NDA 17-354
NDA 17-875	NDA 17-355
NDA 17-876	NDA 16-766
NDA 16-746	NDA 16-854
NDA16-852	NDA 13-554

INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

☐ THIS SUBMISSION IS A FULL APPLICATION (21 CFR 314.50) ☐ THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) (21 CFR 314.55)

IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG

HOLDER OF APPROVED APPLICATION

STATUS OF APPLICATION (Check one)

PRESUBMISSION
☐ ORIGINAL APPLICATION

☒ AN AMENDMENT TO A PENDING APPLICATION
☐ RESUBMISSION

☐ SUPPLEMENTAL APPLICATION

PROPOSED MARKETING STATUS *(Check one).*

☐ APPLICATION FOR A PRESCRIPTION DRUG PRODUCT *(Rx)*

☐ APPLICATION FOR AN OVER - THE - COUNTER PRODUCT *(OTC)*